Resilience as molecular enhancement: bio-economies and medical countermeasures in the United States

Article (Accepted Version)

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Abstract

How have advances in the molecular sciences reshaped our understandings of resilience? This article argues that a novel form of resilience emerges out of the US government's response to the threat of bioterrorism. This response has focused on the development and stockpiling of new pharmaceutical defences known as medical countermeasures. Medical countermeasures allow the body to 'bounce back' from an attack by enhancing at a molecular scale. The obstacles involved in reshaping molecular life into viable countermeasures has led to the creation of a government backed bio-economy formed of public-private partnerships. In doing so, the US government has taken on an extended role accepting the risk that arises in this area. The result is a new scale at which resilience can be implemented and in contrast to many conclusions in the field of International Relations, the responsibilisation of the state rather than citizens in the face of crises.

Keywords

- Resilience
- Molecular life
- Bioterrorism
- Bio-economies
- Medical countermeasures

Significantly, resilience, today, has become something that can be engineered into systems, organisations, perhaps nations and persons.

Lentzos and Rose 2009, 243.

Introduction

Resilience has recently emerged as a specific mode of evaluating life in response to actual and potential disasters, conflicts and catastrophe (Zebrowski 2016, 3). A central concern in this evaluation is the ability of subjects and societies to 'bounce-back' from an unexpected event (see Coaffee 2013; Reid 2012; Malcolm 2013; Welsh 2014; Chandler 2013; O'Malley 2010; Beier 2015; Evans and Reid 2014). In International Relations, this ability has been studied in relation to understandings of responsibility between the state and the individual. The US government has set out to ensure the resilience of its population in the face of a deliberate biological attack through medical preparedness (Homeland Security Council 2007, 27; The White House 2018, 7). This preparedness response is focused on the development and stockpiling of a range of new pharmaceutical defences known as medical countermeasures (MCMs) (Homeland Security Council 2007, 27). A core element in the development of MCMs is the molecularisation of biology and consequently our ability to overcome significant technical and financial obstacles in the re-shaping of life at the molecular level. This article investigates how our understanding of resilience changes as a result of molecular biopolitics. It argues that a novel form emerges, one that enhances the workings of the body to 'bounce back' from potential attack at a molecular scale. Investigations into preparedness efforts have argued that they also generate responsibility (Lakoff 2017, 15). In the facilitation of this form of resilience and medical preparedness this article demonstrates the way that the US government has to intervene to overcome these technical and financial obstacles in the formation of bio-economic relations, taking on an extended and responsibilised role. Resilience as molecular enhancement is intimately tied to the political and economic support mechanisms provided by the US government that ensure the advances in molecular biology can be capitalised upon.

A key conclusion of studies on resilience in International Relations has been the assertion that it is the responsibility of citizens rather than the state to prevent and prepare for disruptive challenges (Coaffee 2013, 248). Risk has been responsibilised away from the state on to individuals and institutions (see Welsh 2014, 15; Coaffee, Murkami- Wood, and Rogers 2008; Lentzos and Rose 2009; O'Malley 2010; Beier 2015). Connectedly and tied in with the neoliberal rollback of the state, resilience is increasingly seen as a quality that individuals acquire largely for themselves without dedicated state support or intervention (Reid 2012 cited in Coaffee 2013, 248). Furthermore, it has

been argued that discourses of resilience do not centrally focus upon material attributes, that resilience concerns attributes which cannot be directly provided by state authorities and that discourses of resilience do not fit well with traditional liberal framings of security practices as state-centric (Chandler 2013, 211). This article contests these conclusions by demonstrating the way that the US government, in protecting its population against bioterrorism through the creation of MCMs, is directly responsible for a form of resilience that enhances the workings of the human body at a molecular scale. In facilitating resilience as molecular enhancement the state has provided support to private companies to overcome technical and financial obstacles, extending itself into the MCM development pathway and taking on risk that is traditionally carried by private industry. Crucially, in contrast to the conclusions noted above, resilience as molecular enhancement is a material attribute directly provided by state authorities.

This argument is made in the following way. It has two sections linked by the molecularisation of biology. Through an analysis of one MCM, the anthrax antitoxin *Raxibacumab*, the first section details a new form of resilience as molecular enhancement. An empirical investigation into the field of molecular biology and the workings of this MCM demonstrates the way that *Raxibacumab* facilitates the 'bouncing back' from an anthrax infection through the provision of readymade antibodies that enhance the body at a molecular scale. This form of resilience is analysed in comparison with other understandings of enhancement in the field and work on immunitary logics. The development of *Raxibacumab* and indeed the entire MCM enterprise is premised upon advances in the life sciences, particularly the molecularisation of biology. Tools such as x-ray crystallography and gene editing have made possible the visualisation and manipulation of life at a molecular scale. Private industry must be able to profitably harness these tools in the creation of viable new products. Yet there are considerable obstacles to this endeavour that have resulted in significant government intervention into this area.

The second section of this article details the way that the US government has had to intervene in the MCM development pathway to overcome these obstacles and ensure that private companies can profitably reshape life at a molecular scale. This has been done through the creation of a bio-economy made up of public-private partnerships. Drug development in general is a lengthy, arduous and extremely costly process with one out of every 5,000 potential compounds ever making it to market (Tucker 2009, 227). The high level of technical risk involved in the process means that development takes between eight and ten years with costs rising to more than $800 million over this period (Tucker 2009, 227). As there is no commercial market for MCMs, without significant state intervention and the provision of support to private companies in two key areas, the first being financial with the second being technical, MCM production would not take place. The Biomedical

Advanced Research and Development Authority or BARDA is a government institution dedicated to providing private companies with financial and technical support in the advanced-development stages of MCM production. Without this support the obstacles to MCM production could not be overcome and the advances in the molecularisation of biology could not be capitalised upon profitably by private companies. As will be argued, the US government through BARDA, in providing support in these two areas has also shielded private companies from the considerable risk that arises in the production of these security technologies. These efforts demonstrate the extension of the US state into MCM development and the governmental responsibilisation of risk in this area. Resilience as molecular enhancement then is intimately tied to advances in molecular biology and the political and economic support mechanisms provided by the US government that ensure these advances can be capitalised upon. This article concludes with the implications of this analysis for our understanding of resilience in the context of molecular biopolitics and the protection of populations against health-based threats.

Resilience as molecular enhancement

What are the implications of this new range of pharmaceutical defences known as MCMs for our understandings of resilience? This section identifies in the workings of a particular MCM a new form of resilience that enhances the body's ability to bounce back from an infection at a molecular scale. In the US government's National Strategy for Homeland Security of 2007 the resilience of the nation's critical infrastructure in the face of terrorist threats is ensured through medical preparedness (Homeland Security Council 2007, 27). Specifically in the face of biological threats, be they naturally occurring or deliberate, access to the necessary MCMs have become essential to the mitigation of vulnerability (Homeland Security Council 2007, 29). In order to facilitate access to these security technologies, the US government has developed an entire operation dedicated to this goal entitled the Public Health Emergency Medical Countermeasures Enterprise (see Elbe, Roemer-Mahler, and Long 2015). Such efforts seek to develop and stockpile various pharmaceuticals including vaccines, antivirals and antitoxins that in protecting the US population from biological agents, ensures the resilience and continued functioning of critical infrastructure in the face of such an attack. A detailed empirical investigation into the workings of particular MCMs such as the anthrax antitoxin *Raxibacumab* will identify a new form of resilience, one that works by actually enhancing at a molecular scale. The political need for a new antitoxin effective against anthrax would only become clear to the US government after the attacks of 2001 and the anthrax letters.

The anthrax letters and the need for new MCMs

Shortly after the attacks of 11 September 2001 letters filled with the biological toxin *Bacillus anthracis* were disseminated through the US postal services. The US government responded with the distribution of the antibiotic ciprofloxacin also known as Cipro. Cipro, manufactured by the Bayer Corporation, is authorised for the off-label use of the treatment of anthrax caused by the inhalation of the *Bacillus anthracis* spores. Entirely reliant upon Cipro to protect its population, the government pressured Bayer to lower the price of the drug. To ensure that Bayer complied the company was threatened with the implementation of 'compulsory licensure'. Such a determination allows for the breach of intellectual property rights in order to benefit society, particularly in regard to property 'affected with a public interest' (Resnik and De Ville 2002, 32–34). Caught short in its dependence upon a single drug to combat bioterrorism and the threat of anthrax, the US government set out to develop additional countermeasures. Legislation in the form of the Project BioShield Act and institutions such BARDA were set up in 2004 and 2006 respectively. BARDA, through public-private partnerships has spearheaded efforts to develop a new next-generation anthrax vaccine and an antitoxin.

The political need for a new vaccine has arisen as a result of the fact that the current one – BioThrax – must be administered well before a person is exposed to *Bacillus anthracis* spores (Borio and Gronvall 2005, 103). While vaccination is extremely useful in protecting security and health personnel that form part of a response mechanism (Borio and Gronvall 2005, 103), the time needed to implement this approach offers up a significant window of vulnerability when trying to protect the general population after an attack has occurred. This lag period can be addressed through the stockpiling of a pharmaceutical defence known as an antitoxin. Antitoxins neutralise the harmful toxins produced by *Bacillus anthracis* that may already be circulating inside a patient's body, immediately addressing any potential infection. This particular type of pharmaceutical also has political value in that it can combat antibiotic-resistant strains of *Bacillus anthracis*, be useful in cases where patients had been exposed to the bacteria before antibiotics could be administered and where exposure was so large as to overcome the protection offered by the vaccine (Danzig 2003, 9).

The significant limitations of antibiotics and the BioThrax vaccine in responding to an attack stimulated political calls for improvements to these defences and government investment in the development of new antitoxins (Danzig 2003, 9). One such antitoxin championed by the US government was *Raxibacumab*, the workings of which provide immediate protection against any infection caused by *Bacillus anthracis*. Crucial to the development of any new MCM, though, is our ability to intervene in and re-shape life at a molecular scale. Such an ability is a direct result of the

advances that have been made in the life sciences in general and the molecularisation of biology in particular.

Raxibacumab and the molecularisation of biology

As is now well known, during the 17th and 18th centuries, in conjunction with the development of capitalism, the growth of the human sciences represented one dimension of the entry of life into history 'that is, the entry of phenomena peculiar to the life of the human species into the order of knowledge and power, into the sphere of political techniques' (Foucault 1998, 141–2). For the first time in history, the classificatory intelligibility (Dillon and Lobo- Guerrero 2009, 2–3) of the biological existence of the human species was reflected in political existence, generating a new form of power – biopower. In conjunction with correlative technologies, life was made amenable to political influence at two different poles and scales – at the level of the human body and that of the population. For the sociologist Nikolas Rose the molecularisation of biology has introduced a molecular gaze into the life sciences (Rose 2007, 12). A molecular scale now joins that of the body and the population in coming to dominate the way medicine functions and is understood. Biomedical research identifies the dynamics of life in terms of functionalities. The differing aspects of molecular life are set out in terms of their particular mechanical and biological properties. Technologies are central to this identification and the visualisation and manipulation of life at the molecular level.

The molecularisation of biology has provided the foundation for the production of a range of new medicines. This ability depends upon that fact that we can now see life in its molecular dimensions and selectively intervene upon it. The first microscopes identified microbes and microorganisms as distinct organisms but it wasn't until the 1930s that the molecular structure of biological organisms was revealed at the sub-microscopic region between $10^{-}6$ and $10^{-}7$ (Kay 1996, 5). Tools such as x-ray crystallography made possible the visualisation of the molecular structure of DNA. This was a crucial step in the discovery in 1953 that the DNA molecule exists in the form of a three-dimensional double helix (Pray 2008, 100) and as a result its function could be discerned from its structure. DNA sequences visualise life in terms of manipulable strings of information. Yet visualisation alone cannot open up the vitality of life at the molecular level to intervention and manipulation.

The gene was opened up to knowledge and manipulation through a number of technologies including DNA binding dyes, restriction enzymes, electrophoresis, radioactive markers and polymerase chain reaction which produced large amounts of short stretches of DNA (Rose 2007, 14).

Our ability to understand and manipulate DNA has introduced modern techniques of molecular genetics such as rational vaccine design (Hanley 2011, 640). Understanding the molecular biology of a virus such as smallpox supports the genetic engineering of attenuating mutations (Hanley 2011, 640). Such mutations are engineered into a recombinant genome that, when inserted into a cell generates a recombinant and attenuated (weakened) virus (Hanley 2011, 640). The ability to recombine genetic material in the formation of new medicines such as vaccines and monoclonal antibodies such as *Raxibacumab* has emerged in correlation with molecular biology's promise to reveal and understand disease processes at the molecular (genetic) level and to determine the optimal molecular targets for drug intervention (Drews 2000, 1962). In other words, our ability to shape molecular life is nothing without an understanding of its inherent or natural processes and dynamics. This understanding has not only facilitated the development of new medicines but in doing so it has also made possible the development and implementation of political programmes of preparedness employed by the US government and directed by organisations such as BARDA to address the threat of bioterrorism.

To address the political need for a new anthrax antitoxin BARDA, with a range of financial and technical mechanisms detailed in the next section, supported the development and stockpiling of *Raxibacumab* through the significant obstacles that beset the production of any new drug. The development of *Raxibacumab* by the private companies Human Genome Sciences and GlaxoSmithKline in coordination with BARDA was possible as a result of the molecularisation of biology. To develop and rationally design a drug, an active molecular site, essential to the disease-causing properties of the pathogen must be recognised as this is what any potential drug will act upon. For example, in order to develop a drug against anthrax we must first understand how the bacteria responsible for the disease – *Bacillus anthracis* – infects and kills human cells. *Raxibacumab* acts only on a specific molecular site of the *Bacillus anthracis* pathogen. Such specific molecular targeting is, again, only possible as a result of particular technologies such as x-ray crystallography.

X-ray crystallography came to prominence after the Second World War as a result of its use in providing conclusive proof of the molecular structure of penicillin (de Chadarevian 2002, 65). X-ray crystallography provided the three-dimensional molecular structure of penicillin from which it was able to determine the active sites essential for its antibacterial function. X-ray crystallography and the X-ray diffraction images produced using this tool were also essential to the discovery of the structure of DNA in the 1950s (Morange 2000, 108). X-ray crystallography exposes a purified and highly concentrated crystal of what is usually a protein to an x-ray beam. When this is done, the resulting image in combination with a computer graphics programme can be used to map the molecular structure of that protein (Smyth and Martin 2000, 8).

An analysis of the proteins that make up the anthrax bacteria using x-ray crystallography revealed one in particular – the protective antigen – that is responsible for the entry of other toxins into human cells. As this protein is responsible for the entry of the other toxins into the cell, preventing this protein from carrying out its function would also prevent the spread of illness within the body. Using x-ray crystallography, the molecular structure and domains or active sites of the protective antigen have been determined. One particular molecular site of the protein – Domain IV – was recognised as the location where the protein bound to the surface of the human cell (Petosa et al. 1997, 833–4). *Raxibacumab* has been designed to bind specifically to this molecular site. In doing so, it prevents the entry of the anthrax toxins from entering the cell and so confers 'passive immunity' to the body by transferring ready-made antibodies that fight the anthrax bacteria on behalf of the patient. Vaccines on the other hand, confer 'active immunity' by exposing the body to live, killed or sub-components of a pathogen and its antigens, so stimulating the body's own production of antibodies to fight infection. The time it takes to stimulate this response is the reason for BioThrax's limitations. *Raxibacumab* once taken by the patient, in contrast to a vaccine such as BioThrax, offers immediate protection against a potential anthrax infection making it a highly valuable political tool in the security response to a bioterrorist attack.

Raxibacumab then provides ready-made antibodies that fight the bacteria on behalf of the patient enhancing the body's response at a molecular scale. The patient, upon taking this particular pharmaceutical, can 'bounce back' from any potential infection and illness. This form of resilience is entirely the responsibility of the state as it is the sole dispenser of MCMs in response to an emergency. This notion of resilience as molecular enhancement has some interesting connections and distinctions to other investigations in the enhancement field.

Resilience and enhancement

Alison Howell has analysed the formulation of resilience in the US Army's Comprehensive Soldier and Family Fitness programme (See Howell 2015a, 15–31; and also, 2015b). Through military psychological resilience training, this programme seeks to assess and instil resilience in soldiers and their families through techniques developed in the discipline of positive psychology. In what has been described as the largest psychological experiment in human history, the theory of learned resilience is positioned as scientific and thus authoritative knowledge (Howell 2015a, 16). The aims of this programme are to produce a fit fighting force in order to wage war more effectively and to reduce healthcare costs and entitlements by claiming to prevent mental health difficulties. With the

reduction of healthcare costs a prime consideration, mental disorders are to be *prevented by enhancing* the happiness of the mass of people it sees 'languishing in life' (Howell 2015a, 25).

Resilience in this case still responsibilises in a neoliberal fashion by off-loading care responsibilities from the state onto the individual or the community by declaring them responsible for their own resilience (Howell 2015a, 24). But for Howell, resilience here does more than just responsibilise. By enhancing human capacities so as to activate happy and mentally agile humans, the negative psychological impacts of unending war and austerity can be withstood and mental disorders prevented (Howell 2015a, 25). Further, through the Global Assessment Tool, a resilience assessment survey, scientific validation has been accredited to the programme. As a consequence, resilience has not only been seen as a scientifically valid way of thinking about the character of soldiers, or human beings more generally, but also that resilience is something that is calculable (Howell 2015a, 26).

The anthrax antitoxin and monoclonal antibody, *Raxibacumab*, molecularly enhances the immune system to fight off the bacteria on behalf of the patient. In this way, in a similar fashion to Howell, illness is *prevented* through *enhancement*. We can, though, distinguish between these forms of resilience as enhancement in terms of temporalities. The resilient subject for Howell must be enhanced *pre-event*, before the negative psychological impacts of unending war and austerity can have their effect (Howell 2015a, 25). In contrast, the stockpiling of antitoxins provides the US government with a preparedness response mechanism to a bioterrorist attack. As routine and preventative vaccination for naturally occurring or deliberate releases of pathogens is no longer a viable policy approach following issues with preventative smallpox and swine flu programmes (See Lakoff 2008), MCMs that can respond immediately and treat infections are highly valued as a political response tool. *Raxibacumab* and other essential medical materiel will be distributed from the SNS *post-event* during an emergency within 12 hours of a federal decision to deploy (Prior 2004, 1) to protect the population from illness and death. Resilience as molecular enhancement in this context is entirely a governmental responsibility and response mechanism. This form of resilience makes an interesting interconnection between biology and politics and it has particular consequences for the work on immunity and the metaphors of infectious disease.

MCMs and the pathogenic immune other

For Colleen Bell the work of Roberto Esposito on the immunitary logic of biopolitics is germane to our understanding of modern counterinsurgency and the medical and biological metaphors used therein (Bell 2012). Twenty-first-century counterinsurgency is a unique entity for Bell, hybrid in

character, involving the convergence of combatants and non-combatants, kinetic and non-kinetic, physical and psychological weaponry, calling on military and civilian expertise and governmental and nongovernmental organisations, that form a wide network of contemporary internationalism (Bell 2012, 225–6). Hybrid warfare exemplifies a double movement of a politics that takes hold of life while also enacting death (Bell 2012, 236). Esposito's 'immunisation paradigm' is so useful in this regard as it captures both the positive, life-supporting aspect of biopolitics alongside its death (or thanopolitical) impulse that has eluded many other biopolitical analyses (Bell 2012, 236–7).

For Esposito biopolitics is inextricably shaped by the struggle between the positive life of the individual, species and community and its negative pathogenic immune other (Esposito 2008, 47). The dialectical struggle between these antonyms, drives history as its productive impulse (Esposito 2008, 47). Esposito, mobilising Hegel (1977, 58–66) demonstrates the way in which identities are generated through the mediated experience of linked yet opposing communities. The paradigm and metaphor of immunisation is used to describe this dialectical relationship. As Haraway notes, the immune system is an elaborate icon for principal systems of material and symbolic 'difference', a map to guide recognition and misrecognition of self and other (1991, 204). When a patient is immunised an attenuated or weakened fragment of the pathogen is introduced against which the immune system must re-cognise and re-integrate, organising defences of a higher form in case of future exposure. So it is with the body politic. The community's exposure to the pathogenic immune – the 'nonbeing' or the 'not-having' – anything in common generates an immunising reaction (Esposito 2008, 51). The community in its exposure to the pathogenic immune is forced to violently overcome it on account of its challenge. Such an overcoming through exposure develops the community into a higher form through this negation. As a result, much like the biological body, as it is immunised it is both preserved in name and changed in content, presupposing that which it also negates (Esposito 2008, 51).

The framing and predominance of thinking around potentially catastrophic events such as bioterrorism in terms of preparedness represents a political recognition that the community will always be violently challenged by its pathogenic immune other. The US government's National Strategy for Homeland Security of 2007 states that 'the future is uncertain and that we cannot envision or prepare for every potential threat, we must understand and accept a certain level of risk as a permanent condition' (Homeland Security Council 2007, 25). In response to this catastrophic imaginary, this strategy notes the importance of 'resilience' as both a strategic and a psychological imperative of national preparedness (Walker and Cooper 2011, 153). In the work of Hayek, the catastrophic event that represents the systemic limits to public management and state planning

(Walker and Cooper 2011, 154), can be reformulated as the inherent need for the community to overcome its pathogenic immune other in the safeguarding of particular forms of life.

In our case, the manipulation of molecular life in the facilitation of resilience as molecular enhancement through the workings of MCMs such as *Raxibacumab*, provides the strategic, medical and prophylactic means from which the population can bounce back from a bioterrorist attack. Zebrowski notes that resilience strategies secure life by enhancing our capacity to quickly adapt and recover from them demonstrating a security logic rooted in ideas of immunity rather than prophylaxis (2017, 219). In this case, prophylactic enhancement, facilitated entirely by the state, is the biological foundation from which a community can respond politically to the exposure to its pathogenic immune other. Yet, such an enhancement requires the manipulation of life at a molecular scale, an endeavour that is notorious for its cost in time, money and expertise, presenting significant financial and technical obstacles. As the next section will demonstrate, this form of resilience would not be possible without an extension and responsibilisation of the state, this time into the MCM development pathway, providing support to companies to overcome these obstacles.

BARDA's bio-economy and the governmental responsibilisation of risk

Resilience and the state

Recent commentary on the role of the state in understanding practices of resilience has noted that 'discourses of resilience do not fit well with traditional liberal framings of security practices as state-centric' (Chandler 2013, 211). Within this, that the very concept of security is 'being shod by liberalism as it embraces not simply forms of endangerment, but a new ideal of resilience' (Evans and Reid 2014, 2). The liberal embrace of contingency and complexity thinking (Evans and Reid 2014, 20) exposes the individual to permanent catastrophes that include environmental change which threaten the natural balance of the world that has sustained our existence to date. Neoliberal governance displaces any sense of social responsibility and pastoral care, naturalising conditions of vulnerability and shifting the burden of security from states to people (Evans and Reid 2014, 65, 74) in the production of a permanently adaptive and self-reliant subject (Evans and Reid 2014, 42, 77). Responsibility for their own safety and security, for their own resilience in the face of crises has been downloaded now from the state onto the individual (Beier 2015, 245). In these understandings, the (neo) liberal state, faced by catastrophes at every turn has withdrawn, exposing life to a challenge to become resilient that also acts as a mode of evaluation (Zebrowski 2016, 3). This article, through a detailed empirical investigation into the way the US state has supported the development of MCMs, will now offer up a contrasting view to that detailed above, one in which security practices in the facilitation of resilience not only remain the responsibility of the state but also require its extension

into novel areas. This extension is a direct result of the difficulty and obstacles that arise in the attempt to reshape life at a molecular scale, obstacles that have contoured the political economy of MCM development in particular ways.

BARDA and MCM development

This article has argued so far that we can identify in the US government's efforts to protect the population from a bioterrorist attack a new form of resilience, one that enhances at a molecular scale. This section demonstrates the way in which the US government has taken on an extended and responsibilised role in the protection of the population against such a threat. In this case, the US state has taken on a considerable share of the risk that arises in the development of MCMs. This is risk that, with more commercially viable products, is usually born by the private sector. This has been done through the provision of financial support and access to key technology. As mentioned the institution focused on working with private companies and providing support in these areas is the Biomedical Advanced Research and Development Authority, otherwise known as BARDA. BARDA, created in 2006, is dedicated to the 'advanced development and acquisition of MCMs to protect the American civilian population against CBRN and naturally occurring emergency threats to public health' (HHS 2007, 17). It has a singular focus on advanced-development as a result of the political, economic and scientific particularities that arise in the MCM development process. It works with private companies and forms bio-economic partnerships that seek to capitalise on our ability to shape life at a molecular scale in the formation of new medicines and MCMs. Such partnerships are essential to ensuring that advances in the molecularisation of biology can be capitalised upon in the constructions of novel forms of resilience.

BARDA was created to overcome the limitations that arose with the first market backed incentive mechanism set up by the US government to encourage private industry participation in MCM development. Funding in the form of the Project BioShield Act dedicated US$5.6bn over 10 years (2004–2013) in what was termed the Special Reserve Fund (SRF). The SRF, the guaranteeing of a federal market for new MCMs, was created to act as a significant incentive for companies to partner with the government in MCM development. This financial incentive was set up to 'artificially' accelerate the development of new MCMs (Elbe, Roemer-Mahler, and Long 2015, 267). As there is little to no natural commercial market for many MCMs, the guaranteeing of a federal market is essential, without which there would be no private-sector investment. Project BioShield funding represented a market guarantee and pull incentive that the US government soon realised would not

be able to attract large and experienced pharmaceutical companies. Opportunity cost was one of the key obstacles that prevented private companies from working in this area.

Project BioShield and its limitations

Drug development is a process focused on the discovery of potential target molecules that have a useful therapeutic effect and that can be marketed in such a way that a return on investment can be assured (Rajan 2017, 38). This process involves taking any potential molecule through the expensive and risky process of clinical trials where many products are rejected. The development of new drugs and vaccines can cost up to $800 million per item and take up to ten years (Hoyt 2012, 27). Further, only one in five drug candidates ever makes it through the extensive clinical studies and trials. The massive amounts of capital investment needed to reshape life at a molecular scale and realise the potential of these products in a process filled with risk and uncertainty has shaped the pharmaceutical industry in particular ways (Rajan 2017, 38).

Traditionally, this risk and potential uncertainty has been mitigated by the massive payoff from extremely profitable blockbuster drugs, molecules that make in excess of a billion dollars a year (Rajan 2017, 39). These drugs offset the high failure rate of potential molecules in the clinical trials process. The profits of this industry are then derived from a small number of compounds, made possible by strong intellectual property protection (Rajan 2017, 40). Commentators such as Mariana Mazzucato, Kaushik Sunder Rajan and Rebecca Hester have noted the significant role that the US government has played in driving innovation and private sector profitability in the pharmaceutical industry (see Mazzucato 2013; Rajan 2006; Hester 2016). This has focused on early stage research often conducted by government organisations such as the National Institutes for Health (NIH) and legislation such as the Bayh-Dole Act of 1980 that allows publicly funded research to be patented for private gain rather than remain in the public domain (Mazzucato 2013, 51). This key piece of legislation was followed six months later by a legal case – *Diamond v. Chakrabarty* – the decision from which (later diminished) set the precedent that genetically engineered organisms, in this case a modified bacterium that could break down oil, could be patented (Hester 2016, 185).

In order to reclaim the money invested in pharmaceutical development, large and experienced firms in the commercial sector command profit margins of 28–31 per cent (Hoyt 2012, 152). In contrast, the profit margins set out under Project BioShield were set at 10 per cent, a common practice in military contracting. Offering profit margins of up to 31 per cent to highly profitable pharmaceutical companies has been noted as being wildly unpopular as well as politically impossible (Hoyt 2012, 156). The monetary incentive and profit margin of 10 per cent was deemed

to be sufficient as it was combined with a range of other factors, such as tax incentives and enhancements along the development pathway such as accelerated regulatory review that would help reduce the cost and risk of MCM development (Hoyt 2012, 152). Despite this being the basis for a reduction in contract prices, the opportunity costs that large and experienced companies faced in the market place have proved to be too high. Large companies, to meet the needs of the government, would have to displace commercially viable and profitable product lines and replace them with biodefence products or invest in new facilities to produce such products (Hoyt 2012, 152). The US government would soon realise that not only were the terms of Project BioShield not attractive to large pharmaceutical companies but also that those same terms would not be enough to support smaller companies through the arduous mid- to late-development stages notoriously known as the 'valley of death'.

VaxGen and the 'valley of death'

One of the most significant factors in MCM development is the lengthy and arduous process that any drug or vaccine must go through before it is considered to be acceptable for human consumption. A particularly notorious aspect of the drug development pathway is known as the 'valley of death'. This refers to the high failure rate of many potential products that arises at the mid- to late-stages of development and in the process of translating basic research into a viable product (slas.org 2011). During this period of transition when a 'developing technology is seen as promising, but is too new to validate its commercial potential and unable to attract the necessary funding for its continued development' (slas.org 2011), many products are abandoned. The phenomenon of the 'valley of death' reflects the high level of cost and risk that occurs in the late stages of MCM development with approximately 60–75 per cent of the overall costs incurred at this point to conduct expensive clinical trials and initiate the start-up of the manufacturing phase (Hoyt 2012, 155).

In 2004, VaxGen, a small biotech company from California, was awarded a $877 million contract to deliver a next-generation recombinant protective antigen (rPA) anthrax vaccine to the US government's SNS. As discussed earlier, it was hoped that this new vaccine could overcome the limitations of BioThrax, the US government's tried and tested vaccine of choice up until that time. After a two-year contract extension VaxGen could still not overcome particular manufacturing issues and the contract was cancelled. Reflection on the reasons for this failure pointed to the limited amount of support that the company could receive under the terms of Project BioShield. With only 10 per cent of a procurement contract available to a company before delivery, when VaxGen ran into technical difficulties, it had to outsource the work at its own cost and did not have access to

sufficient capital resources to continue development. In such a firm, fixed-price contractual arrangement that was set out in Project BioShield's original terms, whilst the developer's market risk is reduced, they assume the significant risk that arises in technical development (Kadlec 2013, 5).

The risk that arises in technical development flows from the uncertain development pathway that leads to the emergence of many unexpected costs. As the procurement contracts under Project BioShield were not subject to adjustment based on the developer's cost experience these unexpected costs place a considerable burden on small companies. Under Project BioShield's terms companies would also not receive compensation or support to mitigate the risk that the product might fail during testing and be undeliverable (Gottron 2014, 2). The US government, following a post-mortem of the VaxGen failure, realised that the risks private companies faced when working in this area represented insurmountable obstacles. In response, BARDA was created to shoulder the burden, to remove the potentially disastrous consequences of product failure from private companies, taking responsibility for the lion's share of the risk, absorbing it within the expertise and financial resources of government. In doing so, public-private partnerships and economic relations have been created to make possible the reshaping of life at a molecular scale into novel forms of resilience.

BARDA's bio-economy – financial and technical support

The lack of participation from experienced private companies in MCM production and the failure of VaxGen highlighted the essential need for the US government to bridge the 'valley of death'. BARDA was created explicitly to do so. Indeed, BARDA's *raison d'être* is to deliver access to funding and technologies that support companies in the manipulation of molecular life essential to the production of MCMs. The lack of federal support in the advanced-development of MCMs, the financial desert that existed between preclinical research supported by the NIH and procurement provided under Project BioShield's SRF (Tucker 2009, 225) would now be populated by BARDA and its financial and technical support. BARDA's financial and technical resources fill this gap by combining Project BioShield's market guarantee and procurement contracts with advanced-development contracts and milestone payments. Milestone payments provide the monetary means for companies to access technical support to ensure MCMs make it through the advanced-development stages that make up the 'valley of death'.

Under Project BioShield companies only had access to 10 per cent of the total procurement contract in advance of the product being delivered to the SNS to cover development studies such as clinical trials. This amount also had to be refunded to the government if the contract was not

fulfilled (HHS 2007, 10). Under BARDA, advanced-development studies could now be supported by contracts that utilised milestone payments. Up to 50 per cent of the total advanced-development contract amount could now be awarded in advance of procurement. These payments would also not be subject to a refund to the US government should the study fail and the contract not be fulfilled (HHS 2007, 10). A considerable share of the risk, particularly that arising in the extremely expensive clinical trial stage, in the 'valley of death' would now be carried by government. These contracts not only represent the way that the US government has accepted a considerable share of this risk but they also allow manufacturers to earn revenues in the development and manufacturing of countermeasures prior to the procurement of the product (Matheny et al. 2007, 232).

Advanced-development contracts have been implemented and awarded in conjunction with technical support mechanisms. Within these partnerships, BARDA has provided private companies with access to technologies essential to critical studies that would usually be found in-house in large pharmaceutical companies. These have focused on what has been termed the Core Services. BARDA's Core Services include the Centers for Innovation in Advanced-Development and Manufacturing, a Fill Finish and Manufacturing Network, a Clinical Studies Network, a Nonclinical Network, a Regulatory and Quality Affairs Division, an Analytical Decision Support Modelling Hub and a Strategic Innovations Portfolio. These services aim to provide core advanced-development and manufacturing services to MCM innovators across a range of issues (Smith 2013) that must be addressed in the development of any successful product. BARDA also provides companies with access to pre-approved companies with which to conduct advanced-development studies such as clinical trials, known as Contract Research Organisations. In the case of clinical trials these companies form a clinical studies network that is ready to respond to requests for the design and execution of Phase I–IV clinical trials on both routine and urgent timelines (Schweinle 2013). Access to such technologies is essential to the successful development of any viable MCM and represents the formation of economic partnerships premised on the shaping of life at a molecular scale (see also Cooper and Waldby 2014).

A bio-economy has been defined as that part of economic activities which 'captures the latent value in biological processes and renewable bio-resources to produce improved health and sustainable growth and development' (OECD 2005, 5 cited in Cooper 2008, 45). Through the creation and implementation of milestone and advanced-development contracts, Core Services and Contract Research Organisations the US government has adapted to overcome the political and economic obstacles that have arisen in MCM development. In doing so they have been able to work with companies to harness the inventiveness of the biotechnology industry in the development of new medicines or MCMs to mitigate the effects of a potential bioterrorist attack. The effect of this has

been the successful completion of a range of public-private partnerships that have not just supported the development and stockpiling of antitoxins such as *Raxibacumab* (and in turn new forms of resilience) but a range of other products to combat other biological threats as well. Indeed, between 2004 and 2014 the US government's bio-economy dedicated to MCM development awarded just over $3bn to the stockpiling of 75 million 25 thousand doses of six MCMs to address the combined threats of smallpox, anthrax and botulism (Gottron 2014, 8). Over the last few years additional funds have been dedicated to stockpile doses of a further two MCMs to combat the threat of anthrax (Hatchett 2016).

It has been argued that a certain logic runs through many state practices supporting resilience, they at once actively intervene and 'step back' to encourage the opening up of new areas to the logic of private enterprise and individual initiative (Joseph 2013, 42). We can see this logic at work in the market guarantee employed in Project BioShield. The position of the state as standing back to encourage private industry in this endeavour was not viable as a result of the particular idiosyncrasies generated in the political economy of MCM development. As a result the US government has not been able to step back. It has had to actively intervene in the advanced-development stages, accepting the financial and technical risk that private industry was meant to bear to ensure that advances in the molecularisation of biology could be capitalised upon. We see here the governmental responsibilisation of risk in the formation of bio-economies that seek to overcome particular obstacles and harness our ability to intervene in the molecular workings of life and the formulation of novel forms of resilience.

Conclusion

This article has investigated how our understanding of resilience changes as a result of molecular biopolitics. The US government's approach to the threat of bioterrorism and in particular the workings of the MCM *Raxibacumab* has revealed a novel form of resilience that facilitates the 'bouncing back' from a potential anthrax infection through the enhancement of the workings of the body at a molecular scale. The molecularisation of life has now fundamentally changed the scale at which resilience can be conceived and implemented. Resilience can literally now be engineered (Lentzos and Rose 2009, 243) into the most fundamental workings of persons and populations. This novel form of resilience has interesting contrasts with other forms of enhancement along the lines of temporality. It is also intimately tied to the political economy of MCM development and the ability to implement advances in the molecularisation of biology. The US government, taking responsibility for the resilience of its population in the face of an anthrax attack has had to create bioeconomic partnerships and support private companies to overcome the financial and technical obstacles

within the MCM development pathway, further demonstrating an extended and responsibilised role. This case has important implications for the field of resilience studies.

Evans and Reid have argued that discourses and practices of resilience are 'intimately tied to neoliberal economic policies, dedicated to developing and protecting neoliberal institutions, including markets and market-based forms of governance' (Evans and Reid 2014, 66). The US government, through Project BioShield, attempted to support companies in MCM development through an entirely market backed mechanism. Its failure has not led to the roll back of the state as is often associated with (neo) liberal economic policy but has required the extension of the US state into the workings of the MCM market. Today has been characterised by the radical depoliticisation of the sphere of the (neo) liberal market economy, a situation that removes it from active discussion and political debate (Žižek 2008, 430). The failure of the market to address the political need for MCMs brings the sphere of the economy into question, politicising it. It also raises a paradox that in order to ensure the resilience of the general population in the face of bioterrorism, to preserve the functioning of the economic and political order in the encounter with its pathogenic immune other; it must also question the functioning of the economy as a political entity. As a result, the US government has had to intervene in the natural regularity and limits of this market in order to incentivise participation and facilitate resilience. This case demonstrates state intervention to address the stark limitations and failures of (neo) liberal market-based governance.

In response to actual and potential disasters, conflicts and catastrophe, resilience has emerged as a specific mode of evaluating life (Zebrowski 2016, 3). This mode of evaluation works in tandem with the responsibilisation of the individual and the shifting of the burden of security from states to people (Evans and Reid 2014, 74). This article has argued that the US state has taken responsibility for a novel form of resilience that does not seek to evaluate life on the basis of its adaptive capacities but enhances its ability to 'bounce back' from a bioterrorist attack. Foucault argued that with the emergence of (neo) liberal forms of govern-mentality the health and welfare of the population became a political priority (2009, 105). Security is now concerned with health and health through tools such as surveillance now becomes focused on security (Weir 2012, 323). Medical preparedness in the face of health-based security threats seeks to sustain life rather than neglect it in the face of incalculable and potentially catastrophic risks. In doing so governments are now able to intervene in the most fundamental workings of their populations in the facilitation of resilience. MCMs represent a significant shift in the scale at which governments can now enhance the resilience of populations in the face of biological threats.

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